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ORIGINAL ARTICLE

Multiple allergies to metal alloys

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ABSTRACT

Background: Metals are well-known allergens that are most commonly encountered as alloys rather than as the pure substance. However, induction of multiple metal allergies by alloys has not been widely reported.
Objective: The aim of this study was to evaluate the prevalence of multiple metal allergies in metal-allergic patients.
Methods: From August 1996 to September 2008, 97 patients (53 females and 44 males) in whom metal dermatitis was suspected were patch tested with the European standard series and a metal series. Age, sex, location of skin rash, occupation, specific metal allergies, and possible sources of sensitization were analyzed.
Results: Positive patch test reactions were seen in 55% (53 of 97) of patients, of whom 21 (40%) were allergic to more than one metal. Nearly three-quarters were sensitized to nickel and to at least one other metal, most commonly palladium, cobalt, or gold. Jewelry, eyeglass frames, watch straps, and buttons were common sources of allergies to multiple metals.
Conclusions: Metal alloys may induce multiple metal allergies. Patients suspected of having a metal allergy should be patch tested with an extended series of metals. We recommend adding palladium and gold, at least, to the standard series.

Introduction

Metals are common allergens that frequently induce contact dermatitis and systemic contact dermatitis.[1,2] The prevalence of allergies to individual metals has been reported in many studies.[3–5] However, people normally have contact with metallic substances in the form of alloys, not pure metals. Such alloys are found in common objects, such as jewelry, eyeglass frames, watch straps, dental restoration, and medical implants. The aim of this study was to evaluate the prevalence of allergies to more than one metal in patients suspected of having a metal allergy.

Patients and methods

From August 1996 to September 2008, 97 patients (53 females and 44 males) who had a history of contact dermatitis to metal were patch tested with the European standard series and a metal series (Chemotechnique Diagnostics, Malmö, Sweden). The test materials are listed in Table 1. We retrospectively reviewed the records of these patients to assess the prevalence of metal allergies and which metals had provoked the sensitivity.

The patch-testing materials were applied in Finn chambers (Epitest Ltd Oy, Tuusula, Finland) covering the upper back with Scanpor tape (Norgesplaster A/S, Vennesla, Norway) and were removed 2 days later. Readings were made on Days 2, 3, and 7, according the protocol recommended by the International Contact Dermatitis Research Group.

Results

Positive reactions to metals were seen in 53 of 97 patients (55%), including 33 women and 20 men (Table 1). Nickel was the most common allergenic metal (37 of 53), followed by chromium (9 of 53), mercury (8 of 53), and gold (7 of 53). There were no positive reactions to aluminum, tin, or zinc.

Allergic responses to more than one metal were seen in 21 of the 53 patients (40%) with metal allergies, including 13 women and 8 men (Tables 2 and 3). The most common combinations were nickel and palladium, nickel and cobalt, nickel and gold, and metallic

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Table 1 Number of patients with positive reactions to each test metal.

Metals	Percent positive reaction					
	Total: 53 (55%, 53/97)		Females: 33 (62%, 33/53)		Males: 20 (38%, 20/53)	
	n	%	*n*	%	*n*	%
Nickel sulfate	37	70	28	85	9	45
Chromate	9	17	1	3	8	40
Cobalt	7	13	5	15	2	10
Gold	7	13	4	12	3	15
Palladium	5	9	5	15	0	0
Copper	3	6	1	3	2	10
Silver	1	2	0	0	1	5
Mercury	8	15	4	12	4	20
Mercuric chloride	4	8	3	9	1	5
Mercury ammonium chloride	6	11	4	12	2	10

Aluminum, tin, zinc: no positive reactions.

mercury and inorganic mercury (Table 4). Nickel-palladium allergy was found mainly in women.

In female patients, jewelry, eyeglass frames, belts, buttons, and watch straps were the major sources of exposure. Skin rashes occurred mainly on the ear lobe, temporal area, wrist, and abdomen, where there was direct contact with metal alloys. They were found to be mainly related to nickel-palladium, nickel-cobalt, and nickel-gold multiple allergies. The men in our study generally had hand eczema as the main clinical manifestation. Nickel and chromate were the most common allergens in them, for whom contact was most frequently occupational, particularly among cement workers; plumbers; and those working with molding, lathes, and electroplating devices. Amount these patients, 40% (8 of 20) had multiple metal allergies, but most of their clinical relevance was unknown.

Discussion

The results of this study showed that allergies to multiple metals are common in metal contact dermatitis. Nickel is the commonest allergenic metal, and nearly three-quarters of multiple metal allergy patients were sensitized to nickel and at least one other metal (15 of 21).

Many commonly used metallic alloys include nickel, which is frequently paired with palladium, gold, or cobalt. Nickel-allergic patients have previously been reported to have palladium and cobalt allergies as well.[6–8] However, it is not clear if this is a matter of cross-reactivity or if it indicates concomitant sensitization.[9,10] In our study, all patients who were allergic to palladium were also sensitized to nickel. Five of the seven cobalt-allergic patients had nickel allergy.

Several metal allergens are found in eyeglass frames, including nickel, palladium, and copper.[11] One of our patients was allergic to all three metals. Overall, nickel was the most common allergen in reactions to eyeglass frames (data not shown).

In a multicenter study of sensitization to dental allergens, ammoniated mercury and mercury (13% and 10.3%) were second only to nickel as the most common allergenic substances.[12] Although some patients in our study were sensitive to various mercury compounds and many of these patients had a past history of dental restoration, no detailed data of the compositions used could be obtained.

Several factors are involved in the potential development of metal-induced allergy. When in close contact with skin for long enough, metals can react with sweat and other body fluids to form a concentration of ions sufficient to initiate an allergic reaction.[13] Jewelry, watch straps, buttons, spectacle frames, belts, and dental alloys commonly meet this condition. Occupational exposure, on

Table 2 Characteristics of female patients with multiple metal allergies.

No.	Age (yr)	Occupation	Location	Trigger items	Piercing	Dental	Allergenic metal
1	19	Student	Face, wrist, abdomen	Belt, watch	+	−	Ni, Au, Co, Pd
2	19	Student	Face	Eyeglass frame	+	−	Ni, Cu, Pd
3	20	Office worker	Ears	Earring	+	−	Ni, Co
4	20	Student	Neck	Earring, necklace	+	−	Ni, Co
5	22	Nurse	Ears, neck, trunk, limbs	Earring, necklace	+	(+) M?	Ni, Co, $HgCl_2$, $HgNH_2Cl$
6	24	Cashier	Hands, feet	NA	−	(+) Hg	Hg, $HgCl_2$
7	29	Hairdresser	Upper eyelids	Eyelash curler	+	−	Ni, Pd
8	31	Computer related	Cheek, chin	Earring	+	(+) M?	Ni, Au, Pd
9	32	Office worker	Abdomen	Button	−	(+) M?	Ni, Pd
10	36	Sales clerk	Neck, wrist, abdomen	Button, watch	−	−	Ni, Cr, Co, Hg, $HgNH_2Cl$
11	39	Nurse	Face	NA	+	(+) M?	Hg, $HgNH_2Cl$
12	39	NA	Trunk, intertriginous area	Thermometer	−	(+) M?	Hg, $HgCl_2$, $HgNH_2Cl$
13	51	Office worker	Neck, wrist	Necklace, watch	NA	NA	Ni, Au

The plus and minus signs in the Column Piercing indicate the patients who "had ear pierced" and "did not have ear pierced" respectively; whereas, in the Column Dental they indicate patients who "had dental alloy" and "did not have dental alloy".
F = female; M? = metals in alloy unknown; NA = not available.

Table 3 Characteristics of male patients with multiple metal allergies.

No.	Age (yr)	Occupation	Location	Trigger items	Piercing	Dental	Allergenic metal
1	23	Welding, molding	Upper limbs, trunk	Cement	−	(+) Ti	Cr, Co
2	24	Plumber	Hands, forearms	Tool handle?	−	(+) M?	Ni, Au, Cu
3	25	Food preparation	Abdomen, neck	Button	−	−	Ni, $HgNH_2Cl$
4	25	Electroplating	Hands, forearms	Electroplate	−	(+) M?	Ni, Au
5	33	Construction	Hands	Tool handle?	−	(+) M?	Ni, Hg, $HgCl_2$, $HgNH_2Cl$
6	40	Metal worker, Cu	Hands	Tool handle?	−	−	Cr, Co
7	47	Cement worker	Hands, forearms, trunk	Cement	−	−	Ni, Cr, Hg
8	48	Construction	Face, neck, limbs, trunk	NA	−	(+) M?	Ag, Hg

The plus and minus signs in the Column Piercing indicate the patients who "had ear pierced" and "did not have ear pierced" respectively; whereas, in the Column Dental they indicate patients who "had dental alloy" and "did not have dental alloy".
? = possible cause; M? = metals in alloy unknown; M = male; NA = not available.

Table 4 Allergies to more than one metal.

Index metal (n/n^a)	Combinations	Index metal (n/n^a)	Combinations
Nickel (15/37)	Ni-Au (2)[b]	Au (5/7)	Ni-Au (2)
	Ni-Co (2)		Ni-Au-Cu
	Ni-$HgNH_2Cl$		Ni-Au-Pd
	Ni-Pd (2)		Ni-Au-Co-Pd
	Ni-Au-Cu		
	Ni-Au-Pd	Co (7/7)	Cr-Co (2)
	Ni-Cr-Hg		Ni-Co (2)
	Ni-Cu-Pd		Ni-Co-Au-Pd
	Ni-Au-Co-Pd		Ni-Co-$HgCl_2$-$HgNH_2Cl$
	Ni-Co-$HgCl_2$-$HgNH_2Cl$		Ni-Co-Cr-Hg-$HgNH_2Cl$
	Ni-Hg-$HgCl_2$-$HgNH_2Cl$		
	Ni-Co-Cr-Hg-$HgNH_2Cl$	Cr (4/9)	Cr-Co (2)
			Ni-Cr-Hg
Metallic, inorganic Hg (9/10)	Hg-Ag		Ni-Cr-Co-Hg-$HgNH_2Cl$
	Hg-$HgCl_2$		
	Ni-$HgNH_2Cl$	Cu (2/3)	Ni-Cu-Au
	Hg-$HgNH_2Cl$		Ni-Cu-Pd
	Ni-Hg-Cr		
	Hg-$HgCl_2$-$HgNH_2Cl$	Pd (5/5)	Ni-Pd (2)
	Ni-$HgCl_2$-$HgNH_2Cl$-Co		Ni-Pd-Au
	Ni-Hg-$HgNH_2Cl_2$-Co-Cr		Ni-Pd-Cu
	Ni-Hg-$HgCl_2$-$HgNH_2Cl_2$		Ni-Pd-Au-Co

[a] Indicates number with multiple metal allergies/number allergic to the index metal;
[b] Indicates a combination found in two patients; all others occurred in only one patient.

the other hand, is becoming less common as operations requiring close contact with metals are becoming increasingly automated, reducing long-term direct contact with skin. Indeed, allergies to occupationally related metals were rare in our study, except in cement workers. Among those exposed, metal tools remain the major sources of occupational metal allergy.

Our study was limited by the small number of patients reviewed. Most were referred with a clear history and clinical manifestations of direct metal contact. Only a few were suspected to have systemic metal allergy–induced diseases with manifestations, such as palmoplantar pustulosis, lichen planus, pompholyx, and general dermatitis. In addition, allergies to dental metallic alloys and medical implants with metal alloy were not well represented in our study population.

Because of the wide variety of alloys used in jewelry, eyeglass frames, watch straps, dental restoration, medical devices, and occupational materials, hypersensitivity to a number of metals is likely underestimated. Metals other than nickel, chromate, and cobalt are rarely included in patch-testing panels, but our study demonstrates that patients suspected of having a metal allergy may actually be sensitive to more than one element of a metallic alloy. Such multiple sensitivities could be identified by using extended series of metals in patch testing. Based on the frequency of allergens in our study, we recommend adding palladium and gold, at least, to the standard series.

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